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REVIEW ARTICLE

Muller misled the Pugwash Conference on radiation risks

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ABSTRACT

The Pugwash Conferences have been a highly visible attempt to create profoundly important discussions on matters related to global safety and security at the highest levels, starting in 1957 at the height of the Cold War. This paper assesses, for the first time, the formal comments offered at this first Pugwash Conference by the Nobel Prize-winning radiation geneticist, Hermann J. Muller, on the effects of ionizing radiation on the human genome. This analysis shows that the presentation by Muller was highly biased and contained scientific errors and misrepresentations of the scientific record that resulted in seriously misleading the attendees. The presentation of Muller at Pugwash served to promote, on a very visible global scale, continued misrepresentations of the state of the science and had a significant impact on policies and practices internationally and both scientific and personal belief systems concerning the effects of low dose radiation on human health. These misrepresentations would come to affect the adoption and use of nuclear technologies and the science of radiological and chemical carcinogen health risk assessment, ultimately having a profound effect on global environmental health.

KEYWORDS

Atomic bombs; cancer; dose response; ionizing radiation; mutation; scientific misconduct

Introduction

On July 9, 1955, Bertrand Russell and Albert Einstein released a manifesto to create a conference for scientists to evaluate the global perils and biological and medical concerns of nuclear weapons. Several days later (July 13th), the industrialist Cyrus Eaton responded to this manifesto, offering to finance and host such a meeting in Pugwash, Nova Scotia, the place of his birth. This first Pugwash meeting was eventually held 2 years later from July 6 to July 11, 1957 (Rabinowitch 1957). A highly select group of scientists (Table 1) attended the first conference from 10 countries with seven scientists from the United States (US), three from the Soviet Union, three from Japan, and one or two from the United Kingdom, Canada, Australia, Austria, China, France, and Poland. Because of the focus on nuclear weapons, most attendees had a background in nuclear physics. The invited participants were supposed to represent themselves instead of the political positions of their respective countries.[1] Since that historically significant July 1957 meeting, the Pugwash conference concept continued and extended in participation and with broader global security issues (Schwart 1967). In 1995, the Nobel Prize was awarded to Dr. Joseph Rotblat for his leadership in enhancing the Pugwash Conference's goals and activities (Rotblat 2001).

Muller and radiation-induced mutation

This paper focuses on the participation and formal remarks of the 1946 Nobel Prize recipient for Biology and Medicine, Hermann J. Muller, a radiation geneticist, at the first Pugwash Conference in Pugwash, Nova Scotia, Canada (Muller 1957). This paper addresses key scientific issues that Muller presented, including their historical and societal context. Within the framework of the Muller invitation and participation, it is important to understand that he had the reputation of being the most distinguished, knowledgeable, and influential geneticist in the world—and one with particular knowledge of the effects of ionizing radiation on the genome. As a result of his extraordinary reputation and the fact that he was unique in his knowledge of matters relating to radiation-induced hereditary disease, Muller's insights

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Table 1. Scientists participating in the first Pugwash Conference (Anonymous 1957).

Name	Affiliation
Cavers, DF	Associate Dean of the Harvard Law School
Chisholm, GB	Physician, Victoria, BC, former Director General of the United Nations World Health Organization
Danysz, M	University of Warsaw, Poland
Doty, P	Department of Chemistry, Harvard University
Kuzin, AM	USSR Academy of Sciences
Lacassagne, AMB	L'Institut du Radium, Paris
Muller, HJ	Nobel laureate in physiology, geneticist and professor of zoology at Indiana University
Ogawa, I	Professor of Tokyo's Rikkyo (St. Paul's) University
Oliphant, MLE	Physicist, director of the Post-graduate Research School of Physical Sciences, National University of Australia, Canberra
Powell, CF	Nobel laureate in physics of the HH Wills Physical Lab at Bristol, England
Rabinowitch, E	University of Illinois, editor of *Bulletin of the Atomic Scientists*
Rotblat, J	Executive vice president of the Atomic Scientists' Association and physics at the University of London
Selove, W	Physicist, University of Pennsylvania
Skobeltzyn, DF	USSSR Academy of Sciences, director of TN Lebedev Institute of Physics, Moscow
Tomonaga, S	Physicist, Tokyo University of Education
Topchiev, AV	Chemist, head of the Institute of Silicates, USSR Academy of Sciences
Thirring, H	Physicist, University of Vienna, author of *Theory of Relativity and Einstein Theory*
Weisskopf, V	Massachusetts Institute of Technology
Yuan, CP	Vice rector of Peking University
Yukawa, H	Nobel laureate in physics and director of the Research Institute for Fundamental. Physics, Kyoto University

Table 2. Selected Muller comments at the Pugwash Conference (Muller 1957).

View on Linearity and Total Dose vs Dose Rate

"Since there is much evidence indicating a linear relation between the radiation dose and the frequency of the induced point mutations, even at extremely low doses, and the exactly cumulative nature of these radiation effects, it becomes possible to arrive at probable estimates of the minimum damage done to subsequent generations of any given chronic or acute exposure of parents." page 2

Radiation Induced Recessive Mutations Lead to Individual and Species Extinction: Genetic Load Hypothesis

" … since the mutant gene is regularly transmitted to subsequent generations, it nearly always results, eventually, in the extinction ("genetic death") of the line of descent carrying it … they represent the price paid by any population in preventing an unlimited accumulation of mutant genes within it … " page 2

Low Doses of Radiation Shorten Lifespan

"It is almost certainly through the individual cell deaths and impairments that minute doses of radiation, long continued or repeated, exert their action in shortening the lifespan of the exposed individual … " page 3

Low Doses of Radiation Induce Cancers in a Linear Dose Response Fashion

" … leukemia and some other malignancies, the induction of which may also be linearly dependent upon radiation dose … " page 3

and remarks would carry exceptional weight in the group's discussions.[2]

Of significance is that Muller had unique access to the most recent findings of the effects of atomic radiation on the offspring of Japanese atomic bomb survivors since a member of the Biological Effects of Atomic Radiation (BEAR) Genetics Panel, James V. Neel, had specifically provided Muller with a major 10-year summary report (Neel and Schull 1956a, 1956b) before its formal release (Calabrese 2020).

Muller's Pugwash remarks

The formal Pugwash remarks of Muller (1957) were based on the contemporary radiation geneticist "mantra" that any exposure to ionizing radiation would cause genetic damage, even a single ionization, and that all such damage was cumulative, irreversible, and not capable of being repaired (Calabrese 2015, 2019a) (See Table 2 for selected Muller comments during his Pugwash Conference Presentation). This widely accepted mantra, at that time, of the effects of ionizing radiation on the genome provided the scientific basis for the creation and adoption of the linear non-threshold (LNT) model for both hereditary and cancer risk assessment.

This perspective that Muller delivered at Pugwash was supported by, and actually an extension of, a major report 1 year earlier (June 12, 1956) by the US National Academy of Sciences (NAS), Biological Effects of Atomic Radiation (BEAR) I Genetics Panel (NAS/NRC 1956), and by a notable paper a year later (May 17, 1957) by future Nobel laureate, Lewis (1957) in the journal *Science*, along with a strong and powerfully influential-editorial endorsement (DuShane 1957) and also with US Congressional Hearings (JCAE 1957) 1 month before the Pugwash meeting. Thus, the timing of the Pugwash meeting, though called for 2 years prior, occurred in excellent synchrony with those major developments in the area of genetic risk assessment and its policy implications. Muller offered key radiation mutation perspectives at Pugwash and played a significant role in affecting perceptions of the effects of low doses on hereditary and cancer risks within human populations.

State of the science when Muller delivered his Pugwash presentation

This paper argues that the presentation of Muller at the Pugwash conference should be seen in a considerably different light today based on a substantial series of historical discoveries over the past decade. These historical findings indicate that some of Muller's comments were based on incorrect information, a profoundly biased perspective, scientific mistakes, scientific misconduct by the US NAS BEAR I Genetics Panel, and a notably flawed paper by Edward B. Lewis (Lewis 1957; Calabrese 2019b, 2021a, 2021b, 2022a).

An example of a recent historical discovery was that key lifetime experimental mouse cancer/longevity study findings of William Russell, at Oak Ridge National Laboratory (ORNL), a member of the US NAS BEAR I Genetics Panel, were deliberately withheld/hidden, which led to the widespread adoption of flawed scientific foundations for the fields of cancer and hereditary risk assessment (Calabrese and Selby 2022). Russell's actions were presumably unknown to Muller at the time of his Pugwash presentation (or ever, for that matter, during his entire career). However, it is important to understand that this type of critical information (i.e., the hidden Russell findings) could have led to different foundational views of the science but were withheld from the US NAS BEAR I Genetics Panel and the attendees at Pugwash. These substantial criticisms of the scientific foundations of cancer and hereditary risk assessment, with particular focus on the LNT dose-response model and Muller's leadership in these activities, have been substantiated, widely presented in the journal literature, recently captured in a 22-episode video historical documentary on LNT and cancer risk assessment by the U.S. Health Physics Society (https://hps.org/hpspublications/historylnt/episodeguide.html).

Thus, this paper is not designed to provide a detailed criticism of the LNT model, as other papers cited here offer that information, analyses, and detailed original references/unique document citations (Calabrese 2015, 2017a, 2019a, 2022b). However, key aspects of these historical findings are critical for they provide a basis to evaluate the accuracy of the information and perspectives that Muller provided during his Pugwash speech. Equally important is that more recently revealed historical findings indicate what Muller failed to share with the Pugwash Conference.

Critical information not shared with the Pugwash Conference

Muller (1927) received great acclaim for being the first to induce gene mutation, reporting these findings in the journal *Science* in July 1927. It was probably little known that the key paper in *Science* provided no data on his discovery, only a discussion of the data. Three months later, Muller would present his findings at the Fifth International Genetics Congress in Berlin. He published the presentation exactly as read in the non-peer-reviewed Congress proceedings (Muller 1928a). The claim that Muller actually induced gene mutations was soon challenged. Muller (1928b) wrote that his friend and colleague Edgar Altenburg demanded to know how Muller knew that he had not simply punched large holes in chromosomes. If this had been the case, there would have been little to no novelty in the Muller findings, and Muller knew this was the case (Muller 1927, 1928b; Campos 2006, starting on page 302). Thus, Muller would strongly try to answer not only the question of his friend, Altenburg, but of many others who questioned the validity of the title of the *Science* paper: "The Artificial Transmutation of the Gene" (Muller 1927). Muller's research centered on trying to show that X-ray-induced genetic changes could induce what he called reverse mutations, in an attempt to show that indeed he had produced only very small point mutations, not gaping holes in chromosomes (Muller 1928b). After many years of research done by multiple groups of researchers, the evidence failed to support Muller (Lefevre 1949, 1950). Eventually, it was determined that Muller confused an observation with a mechanism (Stadler 1954; Crow and Abrahamson 1997) and had not induced point mutations in the gene but rather produced gaping holes in chromosomes.

In a biography written by his last graduate student, it was revealed that the unrelenting criticism of his gene mutation explanation affected Muller, causing him during the last years of the 1930s to doubt that he had induced gene mutation (Carlson 1981). Too much opposing evidence had simply piled up. However, Muller failed to inform the scientific community of his doubts. While Muller would long dispute these challenges to his work, he did eventually admit it in writing, some 10 years after receiving the Nobel Prize for producing gene mutations, that he had not induced gene mutations, as follows: "… there is no doubt that in X-rayed *Drosophila* also, at least when the irradiation is applied to condensed chromosomes states, such as those of spermatozoa, deficiencies as well as other demonstrable structural changes that appear in much higher frequencies relative to changes that appear to involve but one gene…" (Muller 1956).

It is also important to note that the doses that Muller used to induce his chromosome-damaging effects were massive, and they were delivered at a dose rate that exceeded background by about 100,000,000-fold (Calabrese 2019a). At these doses, the normally very resistant fruit flies were often killed and sterilized. Indeed, at these dose rates, the findings had no practical relevance to low dose/dose rate human exposures (Muller 1928a). Yet, when Muller spoke at Pugwash, these limitations were never mentioned.

Despite being on the defensive for most of the 1930s, Muller restored the idea that he had induced gene mutation based on a dissertation that he directed at the University of Edinburgh in 1938–1939 (Ray-Chaudhuri 1939; Calabrese 2011a; Calabrese et al. 2023). As was the case with his groundbreaking findings in 1927, these data were also not subjected to peer review but were published in non-peer-reviewed conference proceedings. Detailed investigations into the nature of the dissertation research, much personal correspondence, and evaluations of the dissertation committee members' comments have revealed many serious shortcomings with this research that were either not reported, masked, or deemphasized (Calabrese 2011a, 2022a). For example, the dissertation/conference proceedings failed to report the location of the incubators used and whether there was lead shielding to prevent control flies from being irradiated by the gamma rays of the radium source. Even if there was lead shielding with 99% efficiency, the control flies would have received about 24 r (0.24 Gy), a massive dose/dose rate in comparison to background radiation exposure. The dose rate would be approximately 80,000-fold background. (Calabrese 2011a; Calabrese et al. 2023). This and numerous other serious flaws have now been discovered, some 70 years after the research. Yet, Muller never shared the research limitations, perhaps because he used the dissertation to rehabilitate his status and to position himself to achieve the Nobel Prize (Calabrese 2011a; Calabrese et al. 2023). When Muller received his Nobel Prize, he strongly praised the flawed dissertation while ignoring a large-scale chronic radiation mutation study with fruit flies by Ernst Caspari that refuted the LNT model and supported a threshold response in which no detrimental health effects were observed at low dose rates (Muller 1946; Calabrese 2011a, 2019a, 2022b). Muller was a paid consultant to the Caspari study and was fully aware of the findings and their research quality before his Nobel Prize Lecture (Calabrese 2015, 2019b). Again, Muller did not share this perspective with the attendees at Pugwash.

Muller also did not share with the Pugwash attendees that his US NAS BEAR I Genetics Panel members had great uncertainty in the evaluation of low-dose radiation-induced genetic risks (NAS/NRC 1956). Upper and lower bound uncertainty estimates considered internally by the committee were massive, by hundreds of thousands for some Panel members, including the 1958 Nobel Prize winner, George Beadle. The uncertainty and the great differences of opinion amongst the Panel members were so extreme that the Panel falsified the research record to hide these issues (Calabrese 2015, 2019a, 2022b). The stated reason was that if the public knew how uncertain the Panel was in its risk assessment of low-dose radiation-induced genetic effects, no one could take any recommendations seriously (See Calabrese 2015, 437, right column). Thus, the Panel published false information to mask uncertainties and to promote policy recommendations.

Muller (1928a) also failed to share with the Pugwash committee that he ridiculed the findings of a 10-year study on the effects of the atomic bomb explosions in Hiroshima and Nagasaki on the offspring of survivors (Calabrese 2020). The problem for Muller with the study of some 75,000 offspring was that the data were negative for adverse genetic effects (and remain so today) (see multiple references in Calabrese 2020). At the BEAR I meeting, Muller called the findings from the 10-year study illusionary and pressured the Panel to not evaluate the human findings (Calabrese 2019a, 2020, 2022b). The major study was led by James Neel (Neel and Schull 1956a,1956b), one of the Panel members. Without the knowledge of the BEAR I Genetics Panel, Neel quietly gave his report to a British Human Population and Genetics Committee of the Medical Research Council that used his findings to derive their public health recommendations. Later in 1956, Muller and Neel would have a major confrontation concerning Neel's sharing of his report with the British Committee. For additional information, see Calabrese (2020).

Several events were happening that Muller was not aware of when he gave the Pugwash presentation that were highly significant, with both relating to the research of William Russell from ORNL. It is now known that throughout most of his career, Russell failed to report data on the occurrence of large clusters of spontaneous mutations in experiments on male mice, which led to a large estimation of control mutation frequency and a resulting large overestimation of

hereditary risks. Indeed, his first experiment, reported in 1951 (Russell 1951), failed to report offspring with the same mutation in a single cluster found in the control group (Selby and Calabrese 2023). This reporting failure of Russell led to the belief that mammals were 15–20-fold more sensitive than *Drosophila*, creating heightened concern for possible human risks, which made the mouse model very significant while enhancing Russell's professional success (Selby and Calabrese 2023). Russell would hide these duplicitous actions over his entire career, only to be revealed some 45 years later, very accidentally, by the inadvertent discovery by Russell's colleague, Selby (2020). This discovery of Selby then led to a major scientific ethics review of the Russell research by an expert panel in 1996 that was mandated by the leadership of the US Department of Energy (DOE). The net result was that the Russells (William and Liane) were told to correct the scientific record in the journal literature. The Russells acknowledged that their estimate of the control mutation rate (specifically the "spontaneous mutation rate per generation") was much too low and provided a correction factor of 2.2, which implied an error of 120% (Russell and Russell 1996; Selby 2020). What this meant in practical terms is that the dose response for the mice in the Russell studies no longer supported an LNT dose response but rather a threshold model (Calabrese 2017b, 2017c) in which there are no detrimental health effects at low doses of radiation but there are effects at higher doses (e.g, a threshold). Had the correct analysis been given to the US NAS Biological Effects of Ionizing Radiation (BEIR) 1970–1972 Committee (National Academy of Sciences/Nuclear Regulatory Commission [NAS/NRC] 1972), the scientific evaluation would almost certainly have indicated the existence of a threshold model, a perspective offered by the US NAS BEAR I Pathology Panel (1956) (Calabrese 2019b). Such a conclusion may have markedly impacted the risk perceptions of the general public, policymakers, and scientific community to ionizing radiation (Selby and Calabrese 2023).

A second hidden story of Russell is that he conducted a large-scale lifespan and cancer risk study in mice that had been exposed to a near-fatal dose of X-rays. This study was designed to confirm a more limited study that suggested that a rather small dose of ionizing radiation could induce a decrease in the lifespan of the offspring of exposed mice. Muller emphasized the Russell (1957) findings of the limited study to the Pugwash committee. Muller never learned (Muller died in 1967 of cardiovascular-related disease) that Russell found no treatment effects on longevity or cancer in the much larger follow-up study, and that Russell hid the findings for 34 years, finally publishing the results in 1993 (Cosgrove et al. 1993), only after being asked to do so by the British nuclear industry to help them win a major court case. Russell claimed that he withheld publishing the negative findings in the manuscript submitted for publication (but not included in the final accepted publication paper) because he did not think that society was capable of properly understanding and processing this information (Calabrese and Selby 2022).

Muller also never shared with the Pugwash audience that the major paper in the journal *Science* by Edward Lewis, some 2 months before the meeting, was terribly flawed in fundamental ways. More specifically, Lewis (1957) estimated leukemia risks in four groups of subjects from radiation exposures. Each of these cases has been shown to have been a distortion of, or inappropriate application of, the data. For example, Lewis (1957) provided leukemia risks of patients based on data that the original investigators explicitly stated should not be used for low-dose cancer risk assessment. Yet, Lewis (1957) did exactly this without sharing this information with the *Science* readership. Lewis manipulated the data of the atomic bomb survivor offspring by combining low and moderate-exposure groups to ensure a linear perspective (Calabrese 2021a). Separating these groups *via* exposure levels showed a J-shaped response characteristic of a threshold model, contradicting the Lewis (1957) paper (see Calabrese (2021a) for the illustration and documentation of the J-shaped dose responses). The fourth group of subjects was radiologists, with Lewis (1957) using very old data, with exposures reaching a massive 2,100 r (21 Gy) (Calabrese 2021a, 2021b).

Discussion

This brief recapitulation of key historical foundations of the LNT history shows that Muller's presentation at the Pugwash Conference was riddled with inaccuracies, scientific misconduct, and ideological bias. Yet, the attendees at Pugwash were led to believe that Muller was the most authoritative person in the world and could provide essential understandings of the biological effects and risks associated with exposures to ionizing radiation concerning mutation, leukemia, and cancer. However, what Muller provided to the group was his highly censored, self-serving, and dishonest views of the status quo (mantra, as described earlier), along with a significant component of inaccuracy that

Muller could not avoid due to the manipulations of Russell. The bottom line is that the attendees at that very first Pugwash meeting were manipulated and misled by the actions of Muller and presented with a distorted view of radiation and low-dose risks, profoundly affecting scientific, political, and societal perspectives. How these distortions affected the formal Pugwash summary report as published in the journal *Science* (Anonymous 1957) and how the distortions affected subsequent Pugwash meetings and the international debate over weapons testing, and partial and full test ban treaty debates, is an area of continuing historical research. However, the perspective that Muller seriously misled the participants at the first Pugwash meeting adds an important new element to this issue.

Yet, the implications of Muller's incorrect interpretations were strikingly important. In 1935, the first mechanistic linear dose-response model for mutation and cancer risk assessment was published (Timofeeff-Ressovsky et al. 1935), which excluded the possibility that cells can repair genetic damage, leading to a likely LNT interpretation (Calabrese 2009, 2011b, 2013, 2018, 2019a, 2022b). This LNT single-hit model was eventually passed on to the U.S. Environmental Protection Agency (EPA) in the early 1970s to guide U.S. cancer risk assessment practices for radiation and chemical carcinogen risk assessment. Thus, the reach of Muller has been profound and long and continues to this day. In his historical appraisal of EPA's carcinogen philosophy, policies, and practices Roy Albert, long-time chair of the EPA Carcinogen Assessment Group (CAG) clearly linked the cancer risk assessment practices of EPA for ionizing radiation and chemical carcinogens to the actions of the NAS BEAR I and BEIR Genetics Panels (Albert 1994).

Conclusion

The above-integrated summary indicates that Muller's presentation at Pugwash was problematic and yet highly important for influencing the knowledge and beliefs of leaders in the radiation field and the media. It shows how uncorrected mistakes, profound bias, scientific misconduct, and other actions, such as hiding data, can adversely affect the education of the public and the scientific community and lead to policies that are not based on the best science. This has been the history of the LNT model for cancer risk assessment over the last 70 years. The presentation of Muller at Pugwash served to promote, on a very visible global scale, these continued misrepresentations of and within the scientific literature and had a significant impact on policies and practices internationally and belief systems concerning the effects of low-dose radiation on human health that would come to affect the adoption and use of nuclear technologies, profoundly affecting global environmental health.

Disclosure statement

The authors declare no conflict of interest.

Data statement

Data sharing is not applicable—no new data generated.

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Notes

1. Muller had a unique perspective as he had lived in the Soviet Union from 1933 to 1937, having then lost his infatuation with the Soviet Union while living under Stalin (Carlson 1981). As Muller would later write: "The problem of living peacefully with them [i.e., Soviet Union] while maintaining our own freedoms is not as simple as he [Cyrus Eaton, organizer and host of the meeting] seems to think" (Carlson 1981, 378, letter from Muller to Randall Hilton October 8, 1959).
2. Even though Muller was perhaps the leading radiation geneticist of his era, he displayed some limitations when it came to predicting the future of his field, something that the Pugwash attendees might have expected or hoped for. For example, in his 1938 letter to Stalin, Muller wrote: "….for it is not possible artificially to change the genes themselves in any particular, specified directions. The idea that this can be done is an idle fantasy, probably not realizable for thousands of years at least" (Glad 2003). In far less than 100 years, society is on the threshold of such developments with CRISPR "gene editing" techniques. This statement is not a criticism that Muller could not predict the future but rather suggests that Muller was not open to other possibilities.

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